Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Regulatory Note

REG2007-02

Azoxystrobin and *Dynasty 100FS Fungicide*

The active ingredient azoxystrobin and the formulated product Dynasty 100FS Fungicide containing 9.6% azoxystrobin for the control of seed- and soil-borne *Rhizoctonia* and *Pythium* spp. causing seed decay, damping-off and seedling blight have been granted temporary registration under the Pest Control Products Regulations.

This regulatory note provides a summary of data reviewed and the rationale for the regulatory decision concerning these products.

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Foreword

Health Canada's Pest Management Regulatory Agency (PMRA) has carried out an assessment of available information in accordance with the Pest Control Products Regulations and has found it sufficient to allow a determination of the safety, merit and value of Dynasty 100FS Fungicide (herein referred to as Dynasty 100FS). The Agency has concluded that the use of Dynasty 100FS in accordance with the label has merit and value consistent with the Pest Control Products Regulations and does not entail an unacceptable risk of harm. Therefore, based on the considerations outlined above, the use of the end-use product Dynasty 100FS for controlling seed- and soil-borne *Rhizoctonia* and *Pythium* spp. is proposed for temporary registration pursuant to the Pest Control Products Regulations.

Methods for analyzing azoxystrobin residues in environmental media are available to research and monitoring agencies upon request to the PMRA.

Syngenta Crop Protection Canada Inc. will be carrying out additional efficacy studies as a condition of this temporary registration. Following the review of this new data, the PMRA will publish a proposed registration decision document and request comments from interested parties before proceeding with a final regulatory decision.

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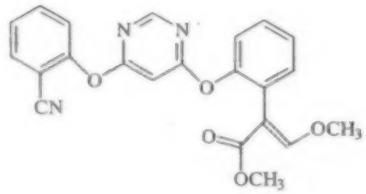
1.0 The Active Substances, Its Properties and Uses

1.1 Identity

Identification of the Technical Grade Active Ingredient

Active substance		Azoxystrobin
Function		Fungicide
Chemical name		
1.	International Union of Pure and Applied Chemistry	methyl (E)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate
2.	Chemical Abstracts Service (CAS)	methyl (E)-2-[[6-(2-cyanophenoxy)-4-pyrimidinyl]-oxy]-α-(methoxymethylene)benzeneacetate
CAS number		131860-33-8
Molecular formula		$C_{22}H_{17}N_3O_5$
Molecular weight		403.4
Structural formula		
Nominal purity of active		96.0% (93.1–98.9%)
Identity of relevant impurities of toxicological, environmental or other significance		The technical grade azoxystrobin does not contain any impurities or microcontaminants known to be Toxic Substances Management Policy (TSMP) Track 1 substances

1.2 Physical and Chemical Properties of Active Substances and End-Use Product(s)

Technical Product—Azoxystrobin

Property	Result	Comment
Colour and physical state	White powder	

Property	Result	Comment
Odour	No characteristic odour	
Melting point or range	116°C	
Boiling point or range	Not applicable	
Density at 25°C	1.25 g/mL	
Vapour pressure at 20°C	1.1×10^{-13} kPa	Relatively non-volatile under field conditions
Henry's law constant at 20°C	7.3×10^{-14} atm m^3/mol $1/H = 3.3 \times 10^{11}$	Low potential to volatilize from water or moist soil surfaces
Ultraviolet (UV) – visible spectrum	Peak maximum at 211 nm. No absorption at > 300 nm.	Low potential for ultraviolet phototransformation in the environment
Solubility in water at 20°C	6.0 mg/L	Low solubility in water
Solubility in organic solvents at 20°C	**Solvent** **100 g/mL** Acetone 8.6 Acetonitrile 34 Dichloromethane 40 Ethylacetate 13 1-octanol 0.14 Methanol 2 Toluene 5.5	
n-octanol–water partition coefficient (K_{ow}) at 20°C	Log $K_{ow} = 2.5$	Unlikely to bioconcentrate or bioaccumulate
Dissociation constant (pK_a)	Not expected to dissociate	
Stability (temperature, metal)	Technical material is compatible with an oxidizing agent (aqueous potassium permanganate), a reducing agent (zinc powder), water and carbon dioxide.	

End-Use Product—Dynasty 100FS

Property	Result
Colour	Opaque yellow
Odour	Paint odour
Physical state	Liquid
Formulation type	Suspension concentrate
Guarantee	100 g/L Nominal (Limits: 95–105 g/L)
Formulants	The product does not contain any PMRA List 1 formulants or formulants known to be TSMP Track 1 substances.
Container material and description	High-density polyethylene (HDPE) bottles.
Density	1.04 g/cm^3 at 20°C
pH	6–9 for a 1% dispersion at 25°C
Oxidizing or reducing action	The product has no oxidizing or reducing properties.
Storage stability	The product was shown to be stable for at least one year under warehouse conditions.
Explodability	The product does not have any explosive properties.

1.3 Details of Uses and Further Information

Dynasty 100FS, with the active ingredient azoxystrobin, is a systemic fungicide formulated as water-dispersible granules. It is proposed to be applied alone or tank mixed with Maxim XL Seed Treatment Fungicide to control seed decay and damping-off caused by *Rhizoctonia* and seed decay, damping-off and seedling blight caused by *Pythium* spp. on popcorn, field, sweet, and seed corn. Dynasty 100FS can also be tank mixed with Cruiser 5FS Seed Treatment Insecticide. Dynasty 100FS is proposed for application at 10 mL/100 kg seed, with a maximum of one application per year.

2.0 Methods of Analysis

2.1 Analytical Methods for Analysis of the Active Substance as Manufactured

Azoxystrobin and the impurities present in the technical product were determined by gas chromatography (GC) with flame ionization detection (FID) detection. The active ingredient and impurities were quantitated using 3-(2-pyridyl)-5,6-diphenyl-1,2,4-triazine internal standard. The

method was shown to be precise with a relative standard deviation (RSD) for the active ingredient of 0.7%, and with a RSD of less than 10% for the impurities. Specificity was demonstrated by the absence of interferences at the retention times of the analytes of interest.

2.2 Analytical Methods for Formulation Analysis

A gas chromatography method was used for the determination of azoxystrobin in the formulation. Quantitation was by internal standard using 3-(2-pyridyl)-5,6-diphenyl-1,2,4-triazine. The method was shown to be linear, precise (RSD of 0.67%) and accurate (mean recovery of 99%). Specificity was demonstrated by the absence of interferences at the retention time of the analyte of interest. The method is acceptable for use as an enforcement analytical method.

2.3 Analytical Methods for Residue Analysis

2.3.1 Methods for Environmental Residue Analysis

The analytical methods for measuring residues in soil and water were previously submitted and found to be acceptable for use as post-registration monitoring methods. In soil, residues of azoxystrobin and the major environmental transformation product, Reference Compound 2, [(E)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylic acid] were determined using high performance liquid chromatography with ultra-violet detection (HPLC-UV); limits of quantification were 0.02 mg/kg for azoxystrobin and Reference Compound 2. In water, residues of azoxystrobin were determined using HPLC-UV detection with a limit of quantification of 1×10^{-4} mg/L.

2.3.2 Multiresidue Methods for Residue Analysis

Azoxystrobin was tested through the Food and Drug Administration (FDA) Multi-Residue Method Test guidelines in PAM Vol. I (dated January 1994). Based on the results, azoxystrobin residues were not adequately recovered in plant or animal matrices under the various multiresidue method protocols tested. However, it should be noted that azoxystrobin can be analyzed using the Canadian Food Inspection Agency's Multiresidue Method [CFIA Volume 7: *Pesticide Multi Residue Analytical Methods Manual* (December 30, 2000)].

2.3.3 Methods for Residue Analysis of Plants and Plant Products

A modified gas chromatography with nitrogen phosphorus detection (GC-NPD) method (RAM 243/06) was developed for the determination of azoxystrobin and the Z-isomer in plant matrices. An alternative high performance liquid chromatography using ultraviolet detection was used for data gathering in vines. Final determination of the residues was also achieved with a high performance liquid chromatography (with electrospray ionization) and tandem mass spectrometry (LC-MS/MS) in representative plant commodities (Method 305/03). The methods fulfilled the requirements with regard to specificity, accuracy and precision at the respective method limit of

quantitation. Acceptable recoveries (70 to 120%) were obtained and adequately bracketed the expected residue levels in representative plant matrices.

2.3.4 Methods for Residue Analysis of Food of Animal Origin

A gas chromatography with nitrogen phosphorus detection (GC-NPD) method (RAM 255/04) was modified for data gathering and enforcement of maximum residue limits in milk, eggs as well as in animal tissues. The method is able to resolve both residues of azoxystrobin and the Z-isomer. In animal matrices, samples are extracted with acetonitrile with clean-up by gel permeation chromatography, prior to elution through Alumina-N and Florisil solid phase extraction cartridges. The method fulfilled the requirements with regard to specificity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70 to 120%) were obtained in representative animal matrices.

3.0 Impact on Human and Animal Health

3.1 Integrated Toxicological Summary (see also: Toxicology Summary Table, Appendix II)

Azoxystrobin administered orally to rats was rapidly and extensively absorbed and distributed into all tissues. Elimination was rapid, mainly in the feces (via the bile), with no evidence of accumulation in tissues. Excretion via expired air was minimal. Repeated oral administration did not alter either the absorption or the excretion pattern. Sex-related differences in excretion and metabolism were minor, although excretion in the urine was slightly higher in females. Biliary metabolites accounted for the greatest amount of absorbed dose in both sexes, mainly at the methoxyacid on the phenylacrylate moiety by hydroxylation and conjugation with glucuronide and, secondly, at the cyanophenyl moiety by hydroxylation and conjugation with glucuronide, glutathione, cysteine, cysteinyl–glycine or mercapturate. Minor amounts of ester cleavage and demethoxylation of the phenylacrylate moiety were observed. No parent compound was detected in the bile or urine. Supplemental plasma absorption studies in nonpregnant and pregnant rabbits showed a similar pattern of rapid absorption and elimination with the methoxyacid metabolite prominent in the plasma and at much higher concentrations than the parent compound.

In laboratory animals, azoxystrobin was of low acute toxicity via the oral and dermal routes of exposure and slightly acutely toxic via the inhalation route of exposure. It was minimally irritating to the eye and skin and not a dermal sensitizer. The end-use product Dynasty 100FS was of low acute toxicity via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eye and skin and not a dermal sensitizer.

In subchronic repeat dosing studies in mice, rats and dogs, the toxicity of azoxystrobin was of a similar order of magnitude following oral administration. The subchronic no observable effect levels (NOEL) for systemic toxicity were 17 mg/kg body weight (bw) per day in mice (90-day) and 20 mg/kg bw/day in rats (90-day), and the overall no observed adverse effect levels (NOAELs) were 25 mg/kg bw/day (1-year) in dogs.

No evidence of toxicity was observed in rats following dermal exposure at a limit dose of 1000 mg/kg bw/day. Toxicity was cumulative in the rat where longer-term exposures produced an increased incidence and severity of pathology at lower effect levels. The chronic NOELs for systemic toxicity were 18 mg/kg bw/day in rats (2-year dietary) and 38 mg/kg bw/day in mice (2-year dietary).

The most common indicators of toxicity were reduced body weight gain, increased liver weight and altered clinical chemistry parameters indicative of an effect on the liver. The principal target organs were the bile duct (rats) and liver (mice, rats, dogs). In rats, increased liver weights and altered clinical chemistry parameters (liver) were observed in males and females with pathology of the bile duct and liver observed in males as cholangitis of the extrahepatic bile duct with proliferation of the intrahepatic bile ducts or ductules and oval cells and either hepatocellular hyperplasia or hepatitis. In dogs, although liver pathology was not observed at the dose levels tested, evidence of an effect on the liver was suggested by the presence of increased liver weights and altered clinical chemistry parameters. In mice, increased liver weight and liver pathology (periportal eosinophilia) were observed in both males and females. Chronic exposure in rats included distension of the common bile duct and marked biliary hyperplasia in the liver. The observed liver and biliary lesions in the rat correlate with the observed high degree of metabolism and biliary elimination. The rat was identified as the most sensitive species in demonstrating liver toxicity.

Gender sensitivity was evident in rats. Male rats exhibited clear pathology of the common bile duct and liver following subchronic and chronic dietary exposures. Furthermore, reduced survival was observed following chronic dietary administration. No such effect was noted in females exposed to similar dose levels; however, some effect was suggested by increased liver weight and altered clinical chemistry parameters. Additionally, published work described a 28-day range finding dietary study in rats where pathology of the bile duct and liver was observed in females at much higher doses.

Azoxystrobin was not oncogenic in rats and mice. Genotoxicity studies indicate that azoxystrobin is not mutagenic in vivo in mammals.

Azoxystrobin was not a reproductive toxicant. A NOEL for reproductive toxicity was 34 mg/kg bw/day based on reduced pup body weight and increased liver weight in F_1 and F_2 litters at the next higher dose level (175 mg/kg bw/day). A NOEL for parental systemic toxicity was 32 and 34 mg/kg bw/day for males and females, respectively; based on reduced body weight and food consumption, increased liver weight and pathology of the liver and bile duct in males at the next higher dose level (165 and 175 mg/kg bw/day in males and females, respectively). No evidence of age-related sensitivity was observed where effects on the offspring of rats and rabbits occurred only at or above maternally toxic doses. In the reproductive toxicity study in the rat, the incidence of bile duct and liver pathology was increased in F_1 males compared with F_0 males; however, the difference was attributed to an increased duration of exposure.

No teratogenic effects were observed in either rats or rabbits exposed to azoxystrobin via oral gavage. The NOAEL for maternal toxicity was 25 and 150 mg/kg bw/day for rats and rabbits,

respectively; based on observed clinical signs and reduced body weight and food consumption. The NOAEL for developmental toxicity in rats was 100 mg/kg bw/day based on a marginal delayed ossification of metatarsals. The NOEL for developmental toxicity in rabbits was 500 mg/kg bw/day (highest dose) in the absence of any observed effects.

Azoxystrobin was not selectively neurotoxic following acute gavage or subchronic dietary administration in rats. The acute NOEL for neurotoxicity is 2000 mg/kg bw/day and the subchronic NOEL for neurotoxicity is 161 mg/kg bw/day. No clinical signs, neurobehavioral effects or pathology of neurological tissues were observed at an acute limit dose of 2000 mg/kg bw or following subchronic dietary administration up to 161 or 202 mg/kg bw/day in males and females, respectively.

3.2 Allowable Daily Intake

The recommended allowable daily intake (ADI) for azoxystrobin is 0.18 mg/kg bw/day. The most appropriate study for selection of a toxicity end point for chronic dietary exposure was the 2-year dietary study in rats, with a NOEL of 18 mg/kg bw/day in males where reduced survival and growth and marked bile duct and liver pathology was observed at and above 34 mg/kg bw/day. The rat was considered the most sensitive species for demonstrating target organ toxicity following subchronic and chronic dietary administration - with evidence of gender sensitivity and cumulative toxicity in males. By applying a 100-fold safety factor to the NOEL (10-fold each for intraspecies and interspecies differences), an ADI of 0.18 mg/kg bw/day was determined.

3.3 Acute Reference Dose

An acute reference dose is not required for azoxystrobin, which is of low acute toxicity by the oral route of exposure. No specific neurotoxicity was observed in the acute neurotoxicity study in rats; however, observed clinical signs in the dog and rat in repeat gavage or capsule studies were attributed to bolus gavage dosing or gastric irritation, or they occurred only at dose levels producing systemic toxicity. No clinical signs of acute toxicity were observed in any of the dietary studies.

3.4 Toxicological End Point for Assessment of Occupational, Residential and Bystander Risks

Short- and Intermediate-term Occupational Dermal and Inhalation Exposures

For acute short- and intermediate-term occupational exposure via the dermal route, the subchronic dermal toxicity study (21-day) in rats with a NOAEL = 1000 mg/kg bw/day was considered the most appropriate. For exposure through the inhalation route for acute short and intermediate term durations, the 90-day dietary rat study with a NOAEL = 20 mg/kg bw/day was considered the most appropriate. The NOAEL is based on decreased body weight, food consumption and utilization, distended abdomen, altered clinical chemistry as well as increased relative liver and kidney weights at 211 mg/kg bw/day (males) and 223 mg/kg bw/day dose levels (females). Moreover, the rat was considered the most sensitive species for demonstrating target organ toxicity following subchronic and chronic dietary administration.

The standard uncertainty factor of 100 is applied to account for intraspecies and interspecies variability. An additional factor for age-related susceptibility is not warranted. Therefore, the target MOE for these scenarios is 100.

Azoxystrobin was of low acute toxicity in rats via the dermal route of exposure and no significant systemic toxicity was observed at a limit dose of 2000 mg/kg bw. In a short-term (21-day) dermal toxicity study in rats, no evidence of toxicity was observed at the limit dose of 1000 mg/kg bw/day where a full range of parameters were investigated including clinical signs, body weight gain, hematology, clinical chemistry and macroscopic and microscopic pathology.

Azoxystrobin was slightly acutely toxic by the inhalation route with an LC_{50} of 0.962 mg/L (males) and 0.698 mg/L (females). Most animals developed slow deep breathing, auditory hypoethesia and breathing irregularities during and up to 4 days post-exposure. Many exposed animals had a splayed gait and reduced splay reflex immediately following exposure.

Azoxystrobin has been shown to be rapidly and extensively metabolized and excreted in the rat with no evidence of bioaccumulation following repeat oral exposures. Significantly less absorption (10-fold) occurred following dermal vs. oral routes of administration.

The dose–response curve for azoxystrobin toxicity has been well characterized in several species (mouse, rat, dog) following subchronic and chronic oral administration. Subchronic oral exposure in all species produced a similar range of effects at comparative effect levels. Chronic toxicity studies showed qualitatively similar toxicity and target organ as in the subchronic toxicity studies and at similar effect levels, although toxicity was cumulative in the male rat following chronic exposure with lower effect levels. Azoxystrobin was not tumorigenic in rats or mice, was not mutagenic or clastogenic in vivo, was not teratogenic in rats or rabbits and was not considered a reproductive toxicant or a neurotoxicant.

3.5 Impact on Human or Animal Health Arising From Exposure to the Active Substance or to Impurities Contained in It

3.5.1 Occupational Exposure and Risk

The end-use product Dynasty 100FS is proposed for use in commercial corn seed treatment facilities.

Based on exposure potential, commercial seed treatment facilities can be classified in two groups: small and large scale. Exposure levels are often higher in small scale facilities; they are often less automated, have fewer engineering controls (ventilation, dust collectors) and use open slurry mixing and transfer systems. Commercial corn seed treatment facilities in Canada can be either small (< 40 metric tonnes of seed treated/day) or large (> 65 metric tonnes of seed treated/day). As such, two different exposure studies were used for the occupational exposure assessment: one for small scale facilities and one for large scale. Data from these studies were considered acceptable to use as surrogate data to assess exposure under the proposed use.

Workers in commercial seed treatment facilities can be classified according to their job function: treater (loading and mixing the product), bagger (bagging the treated seed), sewer (sewing bags), stacker (stacking bags on pallets), forklift driver (moving pallets into the storage area), and worker cleaning, repairing and maintaining equipment. Each of these job functions has different exposure potential and is assessed separately.

For the risk assessment, dermal exposure estimates were compared with the NOAEL of 1000 mg/kg bw/day from the 21-day dermal rat study. Since a dermal NOAEL is used, no dermal absorption value is needed. Inhalation exposure estimates were compared with the NOAEL of 20 mg/kg bw/day from the 90-day dietary rat study. The target margin of exposure (MOE) is 100.

Small-Scale Facilities

Dermal exposure estimates of 0.76 and 0.34 µg/kg bw/day were derived for the treater and bagger/sewer/stacker/forklift driver, respectively.[1] Inhalation exposure estimates of 0.010 and 0.13 µg/kg bw/day were derived for the treater and bagger/sewer/stacker/ forklift driver respectively.[1]

Margins of exposure above 150 000 were achieved for all scenarios and considered acceptable. Exposure estimates and MOEs are summarised in Appendix III.

Large Scale Facilities

Dermal exposure estimates of 0.071 and 0.013 µg/kg bw/day were derived for the treater and bagger/sewer/stacker/forklift driver, respectively.[1] Inhalation exposure estimates of 0.0026 and 0.0039 µg/kg bw/day were derived for the treater and bagger/sewer/stacker/ forklift driver, respectively.[1]

Margins of exposure above 5 000 000 were achieved for all scenarios and are considered acceptable. Exposure estimates and MOEs are summarised in Appendix III.

Workers Cleaning, Repairing and Maintaining Equipment

Margins of exposure were also derived for workers who may have occasional elevated exposures while cleaning, repairing and maintaining seed treatment equipment. The cleaner exposure estimates derived from the surrogate exposure study were 81.98 µg/kg bw/day for the dermal route and 3.12 µg/kg bw/day for the inhalation route.

Margins of exposure above 6000 were achieved and are considered acceptable. Exposure estimates and MOEs are summarised in Appendix III.

Proposed personal protective equipment when treating corn seed should be modified to read:

> Workers who clean-up, maintain or repair seed treating equipment: Wear coveralls over long pants and long sleeves as well as chemical-resistant gloves. For good hygiene practice, a dust mask is also recommended. Workers who treat:

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1 Dermal or inhalation exposure (mg/kg bw/day) = (dermal or inhalation unit exposure × application rate × kg seed treated/day × 1000 µg/mg) / body weight (kg).

Wear long sleeves, long pants as well as chemical-resistant gloves. Workers who bag, sew, stack or drive the forklift: Wear long sleeves, long pants and gloves.

3.5.2 Bystander Exposure

Bystander exposure potential and risk was considered minimal.

3.5.3 Postapplication Exposure

There is potential exposure to individuals planting treated corn seed with Dynasty 100FS.

Planting can be carried out by farmers and custom planters. Custom planters could plant as much as 80 ha in a day whereas farmers can typically plant 40 ha in a day. An exposure study, monitoring both on-farm treating and planting activities, was used to assess planter exposure. This study was considered acceptable to use as a surrogate study and considered conservative to assess the exposure potential under the proposed use. Both the custom and farmer planting treated corn seed were assessed.

For the risk assessment, dermal exposure estimates were compared with the NOAEL of 1000 mg/kg bw/day from the 21-day dermal rat study. Inhalation exposure estimates were compared with the NOAEL of 20 mg/kg bw/day from the 90-day dietary rat study. Since a dermal NOAEL is used, no dermal absorption value is needed. The target margin of exposure (MOE) is 100.

Dermal exposure estimates of 0.11 and 0.056 µg/kg bw/day were derived for custom planter and farmer, respectively.[2] Inhalation exposure estimates of 0.061 and 0.031 µg/kg bw/day were derived for custom planter and farmer, respectively.[2]

Margins of exposure above 300 000 were achieved for all scenarios and are considered acceptable. Exposure estimates and MOEs are summarised in Appendix III.

Proposed personal protective equipment on bag of treated corn seed should be modified to read:

"Use gloves when handling treated seeds."

4.0 Integrated Food Residue Chemistry Summary

4.1 Residue Summary

The metabolism of azoxystrobin in plants and livestock is adequately documented. The metabolic pathway of azoxystrobin was qualitatively similar in the six dissimilar crops evaluated (apple, cotton, grape, peanut, rice and wheat). The metabolic profiles for the target crop were also

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2 Dermal or inhalation exposure (mg/kg bw/day) = (dermal or inhalation unit exposure × application rate × kg seed treated/day × 1000 µg/mg) / body weight (kg).

similar to the profiles found in the rotational crops. The residue definition in plants is azoxystrobin and the Z-isomer. Based on the metabolic profile in laying hens and lactating goats, the residue definition is azoxystrobin and the Z-isomer.

Data demonstrated that the proposed methods are adequate for the analysis of azoxystrobin and the Z-isomer in both animal and plant matrices. The methods were fully-validated in the range of expected residues. Freezer storage of azoxystrobin and the Z-isomer at less than -15°C was confirmed for up to two years in representative fruit/fruiting vegetable crops, non-oily grain crops, and oilseed crops. Residues of azoxystrobin and the Z-isomer were stable at -20°C for one year in poultry tissues (breast/muscle and liver).

Crop field trial data evaluated encompassed the proposed seed treatment use pattern for Dynasty 100FS formulation on field, pop and sweet corn. Forage and kernels plus cob with husks removed were harvested to simulate normal harvest of sweet corn ears and forage. Stover and grain were harvested at maturity. Residues of azoxystrobin and the Z-isomer were less than the limit of quantitation in all corn grain when seeds were treated at the proposed and at exaggerated use rate. An established maximum residue limit (MRL) of 0.03 ppm will cover residues of azoxystrobin and the Z-isomer in corn treated with Dynasty 100FS. Processing data indicated that residues of azoxystrobin and the Z-isomer concentrated 5.9-fold in corn oil and will be covered by the corn oil commodity MRL of 0.2 ppm. Field rotation studies were provided that support current plantback restrictions on respective labels, which indicate 30 days for broadleaf or root crops, and 45 days for cereals grains. Although, there are quantifiable residues in cereal feed fractions, the levels will not impact the potential residues in livestock commodities when the animals are fed a diet consisting of feed items containing azoxystrobin. Adequate feeding studies with azoxystrobin have been reviewed to support the current maximum residue limits for animal commodities.

The proposed domestic use of azoxystrobin in or on corn as a seed treatment does not pose an unacceptable chronic or acute dietary (both food and water) risk to any segment of the population, including infants, children, adults and seniors.

5.0 Fate and Behaviour in the Environment

5.1 Summary of Fate and Behaviour in the Environment

The fate and behaviour of azoxystrobin in the environment have been previously reviewed and reported in Regulatory Note REG2000-15, *Azoxystrobin*.

Azoxystrobin is moderately persistent in aerobic soils and slightly persistent in anaerobic soils with the formation of one major transformation product (Reference Compound 2; (E)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylic acid) and various minor transformation products [Reference Compounds 3 (methyl (E)-2-{2-(6-hydroxypyrimidin-4-yloxy)phenyl}-3-methoxyacrylate); 10 ((E)-2-[2-(6-hydroxypyrimidin-4-yloxy)phenyl]-3-methoxyacrylic acid); 20 (2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-acetic acid); 28 (4-(2-cyanophenoxy)-6-hydroxypyrimidine); 36 ((E)-2-{2-[6-(2-carbamoylphenoxy)pyrimidin-4-

yloxy]phenyl}-3-methoxyacrylic acid)]. Reference Compound 2 undergoes only limited transformation in anaerobic soils. Field studies in Manitoba, Saskatchewan and Alberta (at an application rate of 500 g a.i./ha) indicate that azoxystrobin is nonpersistent to moderately persistent (DT_{50} = 14–62 days); however, DT_{90} values were very long (468 - >738 days) indicating azoxystrobin may be persistent in soils (Appendix IV, Table 1). Measurable residues of azoxystrobin, Reference Compound 2, 28 and 30 (2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]benzoic acid) were detected in soil samples at depths of 0–10 cm only.

Adsorption and desorption tests indicate that azoxystrobin has low to moderate mobility in soils, and Reference Compound 2 has low to very high mobility in soils (Appendix IV, Table 2). Using the Groundwater Ubiquity Score (GUS) assessment method of Gustafson (1989), azoxystrobin is classified as a borderline leacher. Both azoxystrobin and the highly-soluble (solubility: 860 mg/L) Reference Compound 2 may present a risk to groundwater under certain climatic and soil conditions.

Azoxystrobin has low solubility in water, is stable to hydrolysis and may undergo indirect phototransformation via photosensitizors present in aquatic systems. In aquatic systems, azoxystrobin is expected to be persistent and biotransforms to the major transformation product Reference Compound 2 and one minor transformation product, Reference Compound 3.

Although azoxystrobin and the major transformation product Reference Compound 2 are relatively persistent in soil as well as aquatic systems and have properties indicating they may leach in some soils, the very low application rate (0.21–0.32 g a.i./ha) associated with the use of Dynasty 100FS is expected to result in minimal release of azoxystrobin into the environment.

5.2 Expected Environmental Concentrations

The estimated environmental concentrations are initially based on conservative screening level scenarios used to identify products that do not pose a risk. If a risk is identified using the screening level scenarios, then a refined risk assessment is conducted which may include refinement of the estimated environmental concentrations. Where applicable, both the screening level and refined estimated environmental concentrations are reported.

Azoxystrobin is to be applied to corn seed at a rate of 1 g a.i./100 kg seed. Based on information from the Alberta Department of Agriculture, Food and Rural Development, the weight of corn seeds is 380 g per 1000 kernels, the desired plant population of corn ranges from 5–7.6 plants per square metre, and the seeding rate ranges from 21–32 kg seed per hectare. This information was used to calculate the expected environmental concentrations in soil, aquatic systems as well as food.

5.2.1 Soil

Based on the seed treatment rate of 1 g a.i./100 kg seed and a maximum seeding rate of 32 kg seed/ha, the maximum estimated application rate of azoxystrobin is 0.32 g a.i./ha. Using this application rate, and assuming incorporation into the top layer of soil, the concentration of

azoxystrobin in soil was estimated as 0.000 14 mg a.i./kg soil (based on a 15 cm soil depth and soil bulk density of 1.5 g/cm^3).

5.2.2 Aquatic Systems

The aquatic screening level scenario is expected to be very conservative for products used as a seed treatment. Based on the direct application of 0.32 g azoxystrobin/ha to a water body of 30 cm depth, the concentration of azoxystrobin in water was estimated at 0.000 107 mg a.i./L (equivalent to 0.107 µg a.i./L).

5.2.3 Vegetation and Other Food Sources

The treated seed could be consumed directly by birds and wild mammals as a food item. The seed treatment rate (1 g a.i./100 kg seed) and kernel weight (380 g/1000 kernels; 2632 kernels/kg) were used to estimate the amount of azoxystrobin per kernel (0.003 8 mg a.i./kernel). The availability of seeds based on the maximum planting rate was also determined (32 kg seed/ha; 84 224 seeds/ha; 8.42 seeds/m^2). The estimated dietary exposure for different size classes of birds and wild mammals is further described in Section 6.1, Risk Characterization.

6.0 Effects on Non-target Species

6.1 Terrestrial and Aquatic Species

The effects of azoxystrobin and the environmental transformation product Reference Compound 2 on non-target species have been previously reviewed and reported in Regulatory Note REG2000-15 and are summarized as follows:

Azoxystrobin generally showed low toxicity to terrestrial organisms; it is relatively non-toxic to bees and slightly to practically nontoxic to bobwhite quail as well as mallard duck. Azoxystrobin is highly toxic to aquatic invertebrates, moderately to highly toxic to fish and toxic to aquatic plants. The most sensitive aquatic species tested was the freshwater diatom, *Navicula pelliculosa* (NOEC = 20 µg/L). The transformation product, Reference Compound 2, was practically non-toxic to aquatic invertebrates and fish, and was three orders of magnitude less toxic to algae than azoxystrobin. Toxicity endpoints are summarized in Appendix IV, Table 3.

6.2 Risk Characterization

Risk characterization integrates the environmental exposure and ecotoxicology data to estimate the potential for adverse ecological effects. The PMRA conducted a deterministic environmental risk assessment for the corn seed treatment product Dynasty 100FS containing the active ingredient azoxystrobin. The environmental risk was characterized using the risk quotient (RQ) method, which is the ratio of the estimated exposure concentration (EEC) to the appropriate toxicity endpoint (e.g., NOEC) (RQ = EEC/NOEC). For the screening level risk assessment, a RQ < 1 indicates that use of the product is expected to pose a negligible risk (RQ < 0.1) to low

risk (RQ 0.1 to < 1.0), and no further analysis is required. If the screening level risk assessment results in a RQ > 1, then the risk is further refined and characterized.

6.2.1 Environmental Behaviour

Azoxystrobin and the major transformation product Reference Compound 2 are relatively persistent in aquatic and soil systems, and have properties indicating they may leach in some soils. However, the very low application rate (0.21–0.32 g a.i./ha) associated with use of Dynasty 100FS is expected to result in minimal release of azoxystrobin into the environment.

6.2.2 Terrestrial Organisms

Terrestrial plants, earthworms, bees and other beneficial arthropods:

A negligible risk (RQ < 0.1) is expected for earthworms and terrestrial plants (Appendix IV, Table 4), as screening level estimated exposure concentrations (Section 5.2) are well below the NOECs for earthworms and terrestrial plants. A negligible risk is also expected for honeybees and other beneficial arthropods as azoxystrobin is practically non-toxic to honeybees and exposure is expected to be negligible when azoxystrobin is used as a seed treatment.

Birds and Wild Mammals

Birds and wild mammals may be exposed to azoxystrobin through direct consumption of treated corn seed. To characterize this risk, the PMRA considered the likelihood of exceeding the toxic effects endpoints through feeding on treated seed. As an initial screening scenario, risk was characterized for generic small, medium and large size classes of birds and wild mammals. This screening level assessment did not consider variables of feeding preference, availability of treated seed or potential avoidance behaviour toward treated seed and assumed that treated seed would be available for consumption over an extended time period and that 100% of the diet would consist of treated seed.

In order to characterize the risk, both the toxicity endpoints and estimated dietary exposures were expressed as the number of seeds ingested (per day) for each of the generic small, medium and large size classes of birds and wild mammals. Toxicity endpoints were first expressed as a dose (mg a.i./kg bw/day) (Appendix IV, Table 5), and then the most sensitive toxicity endpoint (NOEL) for each exposure period was expressed as the number of seeds ingested (per day) to reach the toxicity endpoint for each size class of birds and mammals (Appendix IV, Table 6). The estimated dietary exposures were determined for each size class of birds and mammals based on estimated daily food ingestion (Nagy, 1987) and assuming 100% of diet consisted of treated seeds (Appendix IV, Table 7).

The risk quotient was determined by dividing exposure by toxicity; where exposure is the estimated number of seeds consumed per day and the toxicity is the number of seeds (per day) required to reach the toxicity endpoint. The risk was then classified based on the risk quotient. As indicated in Appendix IV, Table 8, use of the corn seed treatment is expected to pose a negligible risk to birds and wild mammals. The screening level scenarios indicate that the number of seeds

expected to be consumed per day is well below the toxic effects threshold for all size classes of birds and wild mammals.

6.2.3 Aquatic Organisms

A screening level aquatic EEC (Section 5.2.2) was used to determine if azoxystrobin leaching from treated seed and thus entering an aquatic system could pose a risk to aquatic organisms. As indicated in Appendix IV, Table 9, all risk quotients were less than one (all RQ < 0.006) - indicating azoxystrobin and the major transformation product Reference Compound 2 are expected to pose negligible risk to aquatic organisms through the use of Dynasty 100FS as a seed treatment.

6.3 Risk Mitigation

When used as a corn seed treatment, Dynasty 100FS with active ingredient azoxystrobin is expected to pose negligible risk to terrestrial and aquatic organisms. The product label should, however, include the following environmental precautionary statements:

> This product is toxic to aquatic organisms.
>
> Keep this product out of freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs, ditches and wetlands), estuaries and marine habitats. DO NOT apply directly to aquatic habitats. DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.
>
> The use of this chemical may result in contamination of groundwater, particularly in areas where soils are permeable (i.e., sandy soil) and(or) the depth to the water table is shallow.

7.0 Efficacy

7.1 Effectiveness Against Target Organisms, or With Respect to the Effect Achieved

7.1.1 Intended Use

Table 7.1.1 Proposed Crops, Diseases, Rates and Timing of Application for Dynasty 100FS (Rates provided in mL product and grams of active ingredient per 100 kg seed)

Crop	Disease	Rate
Corn (field, sweet, popcorn and seed corn)	Seed decay and damping-off caused by *Rhizoctonia*; seed decay, damping-off and seedling blight caused by *Pythium* spp.	10 mL/100kg seed (1 g a.i./100 kg seed)

7.1.2 Mode of Action

Azoxystrobin, the active ingredient of Dynasty 100FS, belongs to the strobilurin class of fungicides or Group 11 Fungicides which inhibits mitochondria respiration by impairing electron transfer between cytochrome b and cytochrome c1 at the ubiquinol oxidising site, thereby decreasing energy production at the cellular level.

7.1.3 Crops

Dynasty 100FS is proposed for use on corn including field corn, sweet corn, popcorn and seed corn.

7.1.4 Effectiveness Against Pests

7.1.4.1 Control of Seed Decay and Damping-off Caused by *Rhizoctonia solani*

Three trials conducted on field corn showed that emergence and stand counts for seeds treated with Dynasty 100FS were significantly greater than the inoculated check and not significantly different from the uninoculated check.

All trials compared the proposed rate (1.0 g a.i./ha) with the 0.5-fold and two-fold rates. The data showed that the proposed rate provided numerically higher emergence or stand than the 0.5-fold rate; however, there were no differences when comparing with the two-fold rates. Therefore, the proposed rate of 1.0 g a.i./ha is supported.

The trials also compared Dynasty 100FS alone with tank mix of Dynasty 100FS plus Maxim XL. The data showed that the tank mix of Dynasty 100FS and Maxim XL provided numerically

higher emergence or stand than Dynasty 100FS or Maxim XL alone, but the differences were not significant.

The data support the claims of Dynasty 100FS alone or tank mixed with Maxim XL for control of seed decay and damping-off caused by *Rhizoctonia*.

7.1.4.2 Control of Seed Decay, Damping-off and Seedling Blight Caused by *Pythium* spp.

Two greenhouse trials were submitted for review. Of these, one trial recorded the percentage of seed decay, damping-off and seedling blight. The data showed a significant reduction in seed decay and damping-off by the application of seed treatment; the disease incidence and severity of seedling blight were numerically reduced by the seed treatments. The trial also compared the proposed rate (1.0 g a.i./ha) with the 0.5-fold and two-fold rates. The data showed a positive rate response to the increased rate of azoxystrobin. The 1.0 g a.i./ha rate was determined to be the lowest effective rate. Therefore, the proposed rate of 1.0 g a i./ha is supported.

The trials compared Dynasty 100FS alone with tank mix of Dynasty 100FS plus Maxim XL. The data showed that tank mix of Dynasty 100FS and Maxim XL provided numerically higher emergence or stand count than Dynasty 100FS or Maxim XL alone, but the differences were not significant.

The trail also compared Dynasty 100FS alone with tank mix of Dynasty 100FS plus Maxim XL and insecticide Cruiser 5FS (Reg. No. 27045). The data showed that the addition of Cruiser 5FS did not have any impact in the performance of Dynasty 100FS; therefore, the tank mix with Cruiser 5FS is supported.

The second greenhouse trial showed that Dynasty 100FS alone provided adequate *Pythium* spp. control at the proposed rate. However, only one rating - percentage of stand reduction, was recorded four weeks after planting. The data indicated that azoxystrobin is effective for *Pythium* control at the proposed rate. It did not demonstrate that Dynasty 100FS would provide adequate control for all the proposed claims - i.e., seed decay, damping-off or seedling blight caused by *Pythium* spp.; therefore, this trial is only considered as a supplemental trial.

7.1.4.3 Tank Mix with Cruiser 5FS Seed Treatment Insecticide

Dynasty 100FS (100g/L azoxystrobin) is proposed as a tank-mix on corn with Cruiser 5FS Seed Treatment Insecticide (47.6% thiamethoxam, Reg. No. 27045) and Maxim XL Seed Treatment Fungicide (21% fluduioxonil and 8.4% Metalaxyl-M, Reg. No. 27071) at the registered rates for these products. The data reviewed for the fungicide component of the proposed tank mix indicated that Cruiser 5FS had neither negative impacts on the fungicidal activities of the proposed tank mix nor adverse effects on the crop from of the proposed tank mix.

No data was submitted to support the insecticidal component of the proposed tank mix. However, the efficacy of the insecticide component of the proposed fungicide/insecticide tank mix can be supported based on scientific rationale. Cruiser 5FS has a well-established history of

use on a variety of crops with fungicide tank mixes. No significant adverse effects on the insecticidal activity of Cruiser 5FS were found in the data evaluated for currently registered Cruiser 5FS/fungicide tank mixes and no adverse effects due to these registered tank mixes have been reported. In addition, Dynasty 100FS is marketed in the United States for use in corn only as part of a combination package called Cruiser Extreme Pak, which is a tank mix program combining the seed treatments Dynasty 100FS (1 g a.i./100 kg seed), Maxim XL (3.5 g a.i./100 kg seed), Apron XL (1 g a.i./ha) and Cruiser 5FS (100 g a.i./ha). These application rates are equivalent to the tank mix proposed for the Dynasty 100FS label in Canada.

In light of the lack of any adverse effects on the proposed fungicide component of the tank mix or the proposed crop, the successful history of fungicide tank mixes with Cruiser 5FS for a variety of crops in Canada, and the fact that this tank mix has a history of use in the USA, no significant adverse effects are expected on the insecticidal properties of this tank mix.

7.1.5 Total Spray Volume

Not applicable.

7.2 Phytotoxicity to Target Plants or Target Plant Products

When Dynasty 100FS was applied on field corn at two-fold of the proposed rate, no phytotoxic symptoms were reported. Based on all of the data provided, it is believed that Dynasty 100FS is not phytotoxic to corn.

7.3 Sustainability

7.3.1 Survey of Alternatives

7.3.1.1 Non-chemical Control Practices

Non-chemical disease controls include good crop rotation practices, using high quality seed with rapid seedling emergence and resistance to various seed decay and seedling blight diseases. The standard recommendation for quick germination, emergence and vigorous seedling growth is to plant corn seed 2.5 to 5 cm deep into a firm, moist, well-fertilized and warm seedbed. Any stresses placed on the seed, such as seeding too deeply, using poor quality seed or seeding into cool, wet, too dry or crusted soils will predispose the seedling to disease infection. *Rhizoctonia* and *Pythium* spp. are the main soil-borne pathogens causing seed decay, damping-off and seedling blight.

7.3.1.2 Chemical Control Practices

Table 7.3.1 Alternative Actives Registered as Seed Treatments for Control of the Diseases Listed on the Dynasty 100FS Label

Disease	Active Ingredient	FRAC Group
Soil-borne diseases caused by *Pythium* spp.	Metalaxyl Metalaxyl-M Captan Thiram	4 4 M4 M3
Soil- and seed-borne diseases caused by *Rhizoctonia* spp.	Fludioxonil Captan Carbathiin	12 M4 7

7.3.2 Compatibility with Current Management Practices Including Integrated Pest Management

Azoxystrobin, the active ingredient of Dynasty 100FS, belongs to a different class of chemistry compared to the currently registered seed treatment fungicides. It will offer corn seed companies and their customers a seed treatment product with an alternative mode of action for control of *Rhizoctonia* and *Pythium* spp.

Dynasty 100FS (100 g/L azoxystrobin) is proposed as a tank mix on corn at the registered rates for Cruiser 5FS and Maxim XL. No adverse effects on the insecticidal properties of Cruiser 5FS Seed Treatment Insecticide are expected from this combination.

7.3.3 Contribution to Risk Reduction

Azoxystrobin is a Group 11 Fungicide and it is a new chemical mode of action for use on controlling seed- and soil-borne diseases on corn. The addition of a new fungicide with a different mode of action allows for greater alternation of fungicides, which is part of a successful IPM program and helps in reducing resistance development in fungal populations.

7.3.4 Information on the Occurrence or Possible Occurrence of the Development of Resistance

Azoxystrobin is a Group 11 Fungicide. It has high risk for resistance development. Cross resistance has shown between all member of the Group 11 Fungicides. To delay fungicide resistance:

Where possible, rotate the use of Dynasty 100FS or other Group 11 fungicides with different groups that control the same pathogens.

Dynasty 100FS is a strobilurin fungicide; therefore, continuous or sequential use of within or during successive growing seasons must be avoided or reduced.

Seed treatment use should be based on an integrated pest management (IPM) program that includes scouting, historical information related to pesticide use and crop rotation and considers cultural, biological and other chemical control practices.

7.4 Conclusions

Dynasty 100FS has been demonstrated to be effective in controlling seed- and soil-borne diseases caused by *Rhizoctonia* and *Pythium* spp. on corn (field, sweet, popcorn and seed corn). Dynasty 100FS has not been demonstrated to be non-phytotoxic to corn when applied according to the label directions.

7.4.1 Summary

Table 7.4.1 Summary

Proposed Use Claims	Accepted Use Claims
Crops: corn (field, sweet, popcorn and seed corn) **Disease:** Seed decay, damping-off and seeding blight caused by *Pythium* spp. Seed decay and damping-off caused by Rhizoctonia. **Rate:** 10 mL/100 kg seed For additional disease control, use Dynasty 100FS in combination with labelled rates of Maxim XL. Dynasty 100FS may be tank mixed with Cruiser 5FS insecticide for control of labeled insects. Observe all precautions, limitations, rates and directions for use on the respective labels before applying.	Claims are supported.

8.0 Toxic Substances Management Policy Considerations

During the review of azoxystrobin and Dynasty 100FS the PMRA has taken into account the Federal Toxic Substances Management Policy[3] and has followed its Regulatory Directive DIR99-03.[4] It has been determined that this product does not meet TSMP Track 1 criteria for the following reasons:

- Azoxystrobin is not bioaccumulative. Studies have shown that the *n*-octanol–water partition coefficient (log K_{ow}) is 2.5, which is below the TSMP Track 1 cut-off criterion of ≥5.0.
- Azoxystrobin does not form any major transformation products that meet the TSMP Track 1 criteria.
- Azoxystrobin (technical grade) does not contain any by-products or microcontaminants that meet the TSMP Track 1 criteria. Impurities of toxicological concern are not expected to be present in the raw materials nor are they expected to be generated during the manufacturing process.
- The formulated product Dynasty 100FS does not include any formulants known to contain TSMP Track 1 substances.

9.0 Regulatory Decision

Dynasty 100FS has been granted temporary registration for use on field corn, pop corn, sweet corn and seed corn pursuant to Section 17 of the Pest Control Product Regulations, subject to the generation of two confirmatory trials (small-scale, field/green house) to support the claims for control of diseases caused by *Pythium* spp.

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3 The federal Toxic Substances Management Policy is available through Environment Canada's website at www.ec.gc.ca/toxics.

4 Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, is available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3758; e-mail: pmra_infoserv@hc-sc.gc.ca; or through our website at www.pmra-arla.gc.ca.

List of Abbreviations

ϵ	molar absorptivity
$t_{½}$	half-life
λ	wavelength
ADI	allowable daily intake
a.i.	active ingredient
bw	body weight
CAS	Chemical Abstract Services
d	day
DFR	dislodgeable foliar residue
DT_{50}	dissipation time 50%
DT_{90}	dissipation time 90%
EC_{25}	effective concentration 25%
EC_{50}	median effective concentration
EEC	expected environmental concentrations
F_0	parent generation
F_1	first filial generation
F_2	second filial generation
FOB	functional observational battery
GC	gas chromatography
h	hour
ha	hectare
K_d	adsorption coefficient (ratio of concentration in the soil phase to that in the aqueous phase under test conditions)
K_{oc}	adsorption coefficient (relates K_d to the organic carbon content of the soil sample)
K_{ow}	*n*-octanol–water partition coefficient
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOEC	lowest observable effect concentration
LOQ	limit of quantitation
MOE	margin of exposure
MRL	maximum residue limit
NOAEL	no observable adverse effect level
NOEC	no observable effect concentration
NOEL	no observable effect level
NPD	nitrogen–phosphorus detection
NZW	New Zealand white
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
pK_a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
ROC	residue of concern
RSD	relative standard deviation
TSMP	Toxic Substances Management Policy
TRR	total radioactive residue

Appendix I Food Residue Exposure Assessment Summary

Table 1 Integrated Summary of Residue Data

METHODS FOR RESIDUE ANALYSIS				
Matrix	**Method ID**	**Analyte**	**Method Type**	**LOQ (ppm)**
Plant	RAM 243/06 (supersedes RAM 243/01-243/05) Method 305/03 (supersedes RAM 305/01, 305/02)	azoxystrobin Z-isomer	GC-NPD Alternative HPLC-UV HPLC-MS/MS (*m/z* 404.2→372.4; *m/z* 404.2→343.8)	0.01 ppm for each analyte.
Animal	RAM 255/04	azoxystrobin Z-isomer	GC-NPD	0.01 ppm for each analyte in milk, eggs, liver, muscle, fat.

STORAGE STABILITY OF AZOXYSTROBIN AND Z-ISOMER IN CORN MATRICES			
Matrix	Storage Temp. (°C)	Actual Storage Duration	Demonstrated Storage Stability
Crop Field Trials - Seed treatment RR 99-050B			
Corn forage, grain, stover, kernels plus cob with husk removed	-18 ± 5	54 to 349 days between sampling and extraction; 0 to 14 days from extraction to analysis.	730 days
Crop Field Trials - Seed treatment 2004			
Field corn forage, grain, stover, kernels plus cob with husk removed; sweet corn forage, sweet corn kernels plus cob with husk removed.	-10	Up to 198 days.	730 days

SUMMARY OF RESIDUES FROM THE SEED TREATMENT TRIALS ON CORN WITH AZOXYSTROBIN.									
Crop Matrix	Application Rate (mg a.i./kg seed)	PHI (days)	Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Field, pop, sweet seed corn (proposed use = 1 application at 10 mg a.i./kg seed of Dynasty 100FS (100 g a.i./L). For use in Canada: Do not graze or feed livestock on seeded area for four weeks after planting. Do not use for food, feed or oil processing. For export only: Do not use for food, feed or oil processing.									
Six trials on field corn were conducted in Zone 5 (United States) with a 250 g a.i./L soluble concentrate formulation at 4.3-fold the proposed Canadian label use rate. Kernels plus cob w/husks (CWHR) removed, forage and stover were analyzed to support the use on sweet corn. Samples were analyzed for residues of azoxystrobin and the Z-isomer.									
Azoxystrobin									
K + CWHR	43	-	12	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Forage	43	-	13	0.13	2.7	2.6	0.74	1.04	0.78
Grain	43	-	13	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Stover	43	-	13	0.95	8.7	7.4	3.7	4.33	2.48

Crop Matrix	Application Rate (mg a.i./kg seed)	PHI (days)	Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Z-isomer									
K + CWHR	43	-	12	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Forage	43	-	13	0.01	0.19	0.18	0.03	0.06	0.06
Grain	43	-	13	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Stover	43	-	13	0.02	0.36	0.29	0.13	0.14	0.1
Ten residue trials were completed in Zones 5 (5 trials), 5B (3 trials), 7A (1 trial) and 12 (1 trial) during 2003 using the formulated product azoxystrobin 100 FS. Samples were analyzed for residues of azoxystrobin and the Z-isomer.									
Azoxystrobin and Z-isomer (each analyte)									
Field corn forage	10 20	112–148	166	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	-
Field corn grain	10 20	144–188	166	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	-
Fodder/stover	10 20	144–188	166	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	-
K + CWHR	10 20	60–103	106	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	-
Sweet corn forage	10 20	60–103	106	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	< 0.005 < 0.005	-
SUMMARY OF RESIDUES IN ROTATIONAL CROPS FOLLOWING TREATMENT WITH AZOXYSTROBIN.									
Crop Matrix	Application Rate (g a.i./ha)	PHI (days)	Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Azoxystrobin [80% a.i., WG or 20.8% SC] was applied to leaf lettuce planted in sandy loam or loam soil at a nominal rate of 373 g a.i./ha with 6 applications at two sites (Zone 1 and Zone 10).									
Azoxystrobin									
Lettuce Leaves	2239	30	8	< 0.01	0.01	< 0.01	< 0.01	< 0.01	-
	2239	60	8	< 0.01	0.02	0.015	< 0.01	< 0.01	-
Beet Leaves	2239	30	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
	2239	60	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Beet Roots	2239	30	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
	2239	60	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Wheat - Forage	2239	30	8	0.03	0.13	0.13	0.055	0.069	0.043
	2239	60	8	0.02	0.21	0.16	0.075	0.091	0.078
Wheat - Hay	2239	30	8	0.02	0.12	0.10	0.055	0.059	0.036
	2239	60	8	0.02	0.11	0.10	0.055	0.055	0.036
Wheat - Straw	2239	30	8	0.09	0.18	0.15	0.095	0.11	0.033
	2239	60	8	0.03	0.19	0.18	0.09	0.10	0.060
Wheat - Grain	2239	30	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
	2239	60	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-

Crop Matrix	Application Rate (g a.i./ha)	PHI (days)	Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Z-isomer									
Lettuce Leaves	2239	30	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
	2239	60	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Beet Leaves	2239	30	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
	2239	60	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Beet Roots	2239	30	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
	2239	60	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Wheat - Forage	2239	30	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
	2239	60	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Wheat - Hay	2239	30	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
	2239	60	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Wheat - Straw	2239	30	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
	2239	60	8	< 0.01	0.01	0.01	< 0.01	< 0.01	-
Wheat - Grain	2239	30	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
	2239	60	8	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-

SUMMARY OF RESIDUES IN ROTATIONAL CROPS FOLLOWING TREATMENT WITH AZOXYSTROBIN

Crop Matrix	Application Rate (g a.i./ha)	PHI (days)	Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Azoxystrobin [80% a.i., WG] was applied to cucumbers planted in sandy loam soil at a nominal rate of 224 g a.i./ha, with 7 or 8 applications in total.									
Azoxystrobin									
Mustard Greens	1792	30–36	2	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Turnip - Roots	1792	30–36	2	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Turnip - Tops	1792	30–36	2	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Wheat - Forage	1792	30–61	6	< 0.01	0.02	0.02	0.02	0.02	-
Wheat - Hay	1792	30–61	6	< 0.01	0.01	0.01	< 0.01	0.01	-
Wheat - Straw	1792	30–61	6	< 0.01	0.04	0.04	< 0.01	0.02	-
Wheat - Grain	1792	30–61	6	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Z-isomer									
Mustard Greens	1792	30–36	2	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Turnip - Roots	1792	30–36	2	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Turnip - Tops	1792	30–36	2	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Wheat - Forage	1792	30–61	6	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Wheat - Hay	1792	30–61	6	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Wheat - Straw	1792	30–61	6	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-
Wheat - Grain	1792	30–61	6	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	-

LIVESTOCK FEEDING

The maximum theoretical dietary burdens (MTDB) were calculated using maximum residues observed for feed items in residue trials or established MRLs. The MTDBs are: 70.5 ppm for beef cattle, 51.8 ppm for dairy, 0.47 ppm for poultry and 0.59 ppm for swine.

Table 2 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES			
ROC FOR ENFORCEMENT AND RISK ASSESSMENT **Primary Crops and Rotational Crops**		Azoxystrobin and the Z-isomer	
METABOLIC PROFILE IN DIVERSE CROPS		Similar in six dissimilar crops	
ANIMAL STUDIES			
ROC FOR ENFORCEMENT AND RISK ASSESSMENT		Azoxystrobin and the Z-isomer	
METABOLIC PROFILE IN ANIMALS		Similar in goat, hen and rat	
FAT SOLUBLE RESIDUE		no	
DIETARY RISK from food and water			
Refined Chronic Non-Cancer Dietary Risk **ADI = 0.18 mg/kg bw** **EEC = 99.2 µg/L**	**POPULATION**	**ESTIMATED RISK (% of ADI)**	
		Food	**Food + EEC**
	All infants < 1 yr old	8.1	11.7
	Children 1 to 2 yrs	24.5	26.1
	Children 3 to 5 yrs	19.4	20.9
	Children 6 to 12 yrs	12.9	13.9
	Youth 13 to 19 yrs	7.9	8.7
	Adults 20 to 49 yrs	9.7	10.7
	Adults 50+ yrs	11.8	12.9
	Total Population	11.3	12.4

Appendix II Summary of Toxicology Studies for Azoxystrobin

Toxicokinetics and metabolism: rat Absorption and excretion: rapid and extensive absorption and excretion following oral administration; majority within 48 hours; majority excreted within 48 hours; mainly in feces ((73–89%) compared with urine (9–18%); in bile cannulated rats: bile (72–74%) > feces (15%) > urine (2–7%); minor sex or dose regimen differences Distribution: wide distribution in all tissues by 24 and 48 hours; by day 7 post-dosing, < 1% in tissues and carcass Metabolites: 15 metabolites identified (6 unidentified); minor sex difference; main metabolite a glucuronide conjugate of the methoxyacid on the phenylacrylate moiety (29%); second major group of metabolites included hydroxylation and conjugations of the cyanophenyl moiety (conjugates of glucuronide, glutathione, cysteine, cysteinyl–glycine or mercapturate; < 10% each); minor demethoxylation of phenylacrylate acid moiety and cleavage of ether linkages (< 10% each)			
Acute -Technical			
Oral	Rat (Wistar) (5/sex) limit dose 5000 mg/kg bw	LD_{50} > 5000 ♂♀ no mortality; minimal clinical signs	Low toxicity
Dermal	Rat (Wistar) (5/sex) limit dose 2000 mg/kg bw	LD_{50} > 2000 ♂♀ no mortality or clinical signs, slight erythema	Low toxicity
Inhalation	Rat (Wistar) (5/sex) 0.24, 0.48, 0.72 or 0.97 (♂) mg/L air	LC_{50} = 0.96 ♂ / 0.70 ♀ (mg/L air) mortality at ≥ 0.48 mg/Lair; clinical signs ≥ 0.24 mg/L air	Slight toxicity
Skin irritation	Rabbit (New Zealand white [NZW]) (6 ♀) 500 mg; Draize	Primary irritation $score_{1-72h}$ = 0.41	Minimal dermal irritant
Eye irritation	Rabbit (NZW) (6 ♀) 100 mg; Draize	Maximum average $score_{1h}$ = 4.3	Minimal eye irritant
Skin sensitization	Guinea pig (Dunkin Hartley) Maximization test	negative	Not a sensitizer
Dynasty 100FS Fungicide EUP			
Acute Oral LD_{50} Fixed Dose Method (420)	Rat (Alpk:AP$_f$SD) Dosed at 2000 mg/kg	LD_{50} ♀ = > 2000 mg/kg bw	Low toxicity
Acute Dermal LD_{50}	5 rats ((Alpk:AP$_f$SD)/sex Dosed at 2000 mg/kg	LD_{50}♂♀ > 2000 mg/kg	Low toxicity
Acute Inhalation LC_{50}	5 rats ((Alpk:AP$_f$SD)/sex Dosed at 5.98 mg/L	LC_{50}♂♀ > 5.98 mg/L	Low toxicity
Primary Eye Irritation	3 male (New Zealand White albino) rabbits Dosed with 0.1 mL for 1, 24, 48 and 72 hours	MAS[a] = 1.33/110 MIS[b] = 4/110	Minimal irritation

Primary Skin Irritation	3 rabbits (3 males New Zealand White albino) Dosed with 0.5 mL for 4 hours	MAS= 0.11/8 MIS= 0.33/8	Minimal irritation
Skin Sensitization Buehler	20 female (Dunkin Hartley) guinea pigs/dose 10 for control Dosed with 0.4 mL for 6 hours; 3 inductions, 1 challenge, 1 rechallenge	Ind. = 20%, Chal.= 0% Ind. = 4/20, Ctrl. = 1/10 Chal. = 0/20, Ctrl. = 2/10	Not a sensitizer

Study	Species (strain) and Dose Levels	NOEL or NOAEL (mg/kg bw/day)	Observations
Short-term			
90-d dietary	Mouse (C57BL/10JfAP/Alpk) 0, 100, 1000, 3000 or 7000 ppm [♂ 0, 17, 188, 569 or 1280 mg/kg bw/day] [♀ 0, 21, 227, 675 or 1468 mg/kg bw/day] (10/sex/dose)	17	1280 ♂ / 1468 ♀ all animals sacrificed in extremis week 3 569 ♂ / 675 ♀ ↓ body weight and food utilization, ↑ relative liver weight, liver pathology 188 ♂ / 227 ♀ ↓ body weight ♀, ↓ food utilization ♂, ↑ relative liver weight ♂, liver pathology ♀
90-d dietary	Rat (Alpk:APfSD) 0, 200, 2000 or 4000 ppm [♂ 0, 20, 211 or 444 mg/kg bw/day] [♀ 0, 22, 223 or 449 mg/kg bw/day] (12/sex/dose)	20	444 ♂ / 449 ♀ ↓ body weight, ↓ food consumption and utilization, distended abdomens, altered hematology and clinical chemistry (liver), ↑ relative liver and kidney weights, bile duct and liver pathology ♂ 211 ♂ / 223 ♀ ↓ body weight, ↓ food consumption and utilization, distended abdomens, altered clinical chemistry, ↑ relative liver weight, ↑ relative kidney weight ♀
21-d dermal	Rat (Wistar) 0, 200, 500 or 1000 mg/kg bw/day (5/sex/dose)	≥ 1000	no treatment-related toxicity at highest dose tested

Study	Species (strain) and Dose Levels	NOEL or NOAEL (mg/kg bw/day)	Observations
90-d capsule	Dog (Beagle) 0, 10, 50 or 250 mg/kg bw/day (4/sex/dose)	10	250 ↓ body weight, clinical signs (salivation, fluid feces), altered clinical chemistry parameters (liver), ↑ liver and thyroid weights ♀ 50 ↓ body weight ♀, altered clinical chemistry ♂, ↑ liver weight ♀ 10 altered clinical chemistry ♂
1-year capsule	Dog (Beagle) 0, 3, 25 or 200 mg/kg bw/day (4/sex/dose)	25	200 clinical signs (fluid feces, salivation ♀), altered clinical chemistry (liver), ↑ liver weight 25 altered clinical chemistry ♂, ↑ liver weight ♀
Chronic Toxicity and Oncogenicity			
2-year dietary	Mouse (C57BL/10JfAP/Alpk) 0, 50, 300 or 2000 ppm [♂ 0, 6, 38 or 272 mg/kg bw/day] [♀ 0, 9, 51 or 363 mg/kg bw/day] (55/sex/dose)	38	272 ♂ / 363 ♀ ↓ body weight, ↓ food utilization, ↑ liver weight; not oncogenic
2-year dietary	Rat (Alpk:APfSD) ♂ 0, 60, 300 or 1500 (×52 weeks) + 750 (×52 weeks) ppm [0, 4, 18 or 108–134 mg/kg bw/day] ♀ 0, 60, 300 or 1500 ppm [0, 5, 22 or 117 mg/kg bw/day] (52/sex/dose)	18	108–134 ♂ / 117 ♀ ↓ survival ♂, distended abdomens ♂, hunched ♂, ↓ body weight, ↓ food consumption and utilization, ↓ adrenal and kidney weights, bile duct and liver pathology ♂; not oncogenic
Reproductive and Developmental Toxicity			
Multi-generation reproduction	Rat (Alpk:APfSD) 0, 60, 300 or 1500 ppm [♂ 0, 6, 32 or 165 mg/kg bw/day] [♀ 0, 7, 34 or 175 mg/kg bw/day] (26/sex/dose)	maternal 34 reproductive 34	165 ♂ / 175 ♀ F_0/F_1 adult ↓ body weight, ↓food consumption, ↑ liver weight, bile duct and liver pathology ♂ F_1/F_2 pups ↓ body weight during lactation period, ↑ liver weight

Study	Species (strain) and Dose Levels	NOEL or NOAEL (mg/kg bw/day)	Observations
Teratogenicity	Rat (Wistar) 0, 25, 100 or 300 mg/kg bw/day gd 7–16 (24/dams/dose)	maternal 25 developmental 100	maternal 300 excessive maternal toxicity (discontinued) 100 ↓ body weight, ↓ food consumption, diarrhea, urinary incontinence, salivation 25 salivation developmental 100 marginal delayed ossification; not teratogenic
Teratogenicity	Rabbit (NZW) 0, 50, 150 or 500 mg/kg bw/day gd 8–20 (21 mated/dose)	maternal 150 developmental 500	maternal 500 ↓ body weight, ↓ food consumption 150 transient ↓ food consumption developmental no significant effects; not teratogenic
Neurotoxicity			
Acute neurotoxicity	Rat (Alpk:APfSD) 0, 200, 600 or 2000 mg/kg bw	systemic 600 neurotoxicity 2000	systemic 2000 ↓ body weight ♂ (marginal) ≥ 200 transient diarrhea and gastric irritation neurotoxicity no effect on functional observational battery (FOB), motor activity, brain weight or neuropathology; not selectively neurotoxic
13-week neurotoxicity	Rat (Alpk:APfSD) 0, 100, 500 or 2000 ppm [♂ 0, 8, 39 or 161 mg/kg bw/day] [♀ 0, 9, 48 or 202 mg/kg bw/day]	systemic 39 neurotoxicity 161	systemic 161 ♂ / 202 ♀ ↓ body weight ♂, ↓ food consumption and utilization ♂ neurotoxicity no effect on FOB, motor activity, brain dimensions or neuropathology; not selectively neurotoxic

Mutagenicity	
Bacterial cell gene mutation assay (in vitro) *S. typhimurium* (TA1535, TA1537, TA98, TA100) *E. coli* (WP2P, WP2P uvrA)	negative (±S9)
Mammalian cell gene mutation assay (in vitro) L5178Y mouse lymphoma cells	positive (±S9)
Mammalian cell cytogenetics assay (in vitro) Human lymphocytes	positive (±S9)
Mammalian cell cytogenetics study (in vivo) Mouse bone marrow micronucleus	negative
DNA damage and repair study (unscheduled DNA synthesis) (in vivo) Rat hepatocytes (male)	negative

Appendix III Summary of Occupational Exposure

Table 1 Exposure Estimates and MOEs for Workers Using Dynasty 100FS with Azoxystrobin as the Active Ingredient and Planters Planting Treated Seeds

Small Scale Commercial Corn Seed Treatment Facilities		
Corn Seed	**Treater Exposure**	**Bagger/Sewer/Stacker and Forklift Operator Exposure**
Maximum rate: 1 g a.i./100 kg Amount treated/day: 25 000 kg/day	Dermal: 0.76 µg/kg bw/day [a] Inhalation: 0.010 µg/kg bw/day [a] Dermal MOE: 1 300 000 [b] Inhalation MOE: 1 900 000 [b]	Dermal: 0.34 µg/kg bw/day [a] Inhalation: 0.13 µg/kg bw/day [a] Dermal MOE: 2 900 000 [b] Inhalation MOE: 150 000 [b]
Large Scale Commercial Corn Seed Treatment Facilities		
Corn Seed	**Treater Exposure**	**Bagger/Sewer/ Stacker and Forklift Operator Exposure**
Maximum rate: 1 g a.i./100 kg Amount treated/day: 68 000 kg/day	Dermal: 0.071 µg/kg bw/day [c] Inhalation: 0.002 6 µg/kg bw/day [c] Dermal MOE: 14 000 000 [b] Inhalation MOE: 7 600 000 [b]	Dermal: 0.013 µg/kg bw/day [c] Inhalation: 0.003 9 µg/kg bw/day [c] Dermal MOE: 80 000 000 [b] Inhalation MOE: 5 100 000 [b]
Small & Large Scale Commercial Corn Seed Treatment Facilities		
Corn Seed	**Cleaner Exposure**	
Maximum rate: 1 g a.i./100 kg Amount treated/day: 68 000 kg/day	Dermal: 81.98 µg/kg bw/day [d] Inhalation: 3.12 µg/kg bw/day [d] Dermal MOE: 12 200 [b] Inhalation MOE: 6410 [b]	

Planting Treated Corn Seed		
Corn Seed	**Farmer Exposure**	**Custom Exposure**
Maximum rate: 1 g a.i./100 kg Seeding rate: 24 kg/ha Amount planted/day: 40 ha/day by farmer 80 ha/day by custom planter	Dermal: 0.056 µg/kg bw/day [c] Inhalation: 0.031 µg/kg bw/day [c] Dermal MOE: 18 000 000 [b] Inhalation MOE: 650 000 [b]	Dermal: 0.11 µg/kg bw/day [c] Inhalation: 0.061 µg/kg bw/day [c] Dermal MOE: 9 000 000 [b] Inhalation MOE: 330 000 [b]

[a] Based on the 90th percentile unit exposure value from the surrogate study.

[b] Dermal or inhalation Margin of Exposure (MOE) = (Dermal or Inhalation NOAEL × 1000 µg/mg) / Dermal or Inhalation Exposure (mg/kg bw/day)

[c] Based on the arithmetic mean unit exposure value from the surrogate study.

[d] Based on the maximum unit exposure value of one cleaner from the surrogate study.

Based on 70 kg body weight in all calculations.

The dermal NOAEL is 1000 mg/kg bw/day based on a 21-day rat dermal toxicity study.

The inhalation NOAEL is 20 mg/kg bw/day based on a 90-day dietary rat toxicity study.

Target margin of exposure (MOE) is 100 for both exposure routes.

Appendix IV Environmental Assessment

Table 1 Summary of Transformation of Azoxystrobin

Process	Value	Interpretation
Abiotic		
Hydrolysis (25°C)	pH 5, 7 stable pH 9 $t_{½}$ = 267 d	Hydrolysis is not a major route of transformation in the environment.
Phototransformation in soil (25°C)	DT_{50} = 7.7–14 d	Photolysis is a route of transformation in soil.
Phototransformation in water (25°C)	DT_{50} = 10.7–16.2 d	Direct photolysis is not expected to be a major transformation pathway in aqueous environments.
Phototransformation in river water (25°C)	DT_{50} = 5.2 d	Azoxystrobin may be subject to indirect photolysis in aqueous environments.
Biotic		
Biotransformation in aerobic soil (20°C)	DT_{50} = 54–135 d	Moderately persistent[a]
Biotransformation in anaerobic soil (20°C)	DT_{50} = 36–45 d	Slightly persistent[a]
Biotransformation in aerobic water – anaerobic sediment systems (20°C)	$t_{½}$ = 187–239 d	Persistent[b]
Field Studies		
Manitoba, Saskatchewan, Alberta	DT_{50} = 14-62 d DT_{90} = 468 - >738 d	Nonpersistent to moderately persistent[a]

[a] Persistence classifications based on Goring et al. (1975)

[b] Persistence classifications based on McEwen and Stephenson (1979)

Table 2 Summary of Laboratory Mobility Studies[a]

Soil	Azoxystrobin	Reference Compound 2[b]	Reference Compound 28[c]	Reference Compound 30[c]
Sand (Lilly Field, United Kingdom)	K_{oc} = 710 Low mobility	K_{oc} = 770 Low mobility	—	—
Loamy sand (Kenny Hill, United Kingdom)	K_{oc} = 300 Moderate mobility	K_{oc} = 34 Very high mobility	K_{oc} = 120 High mobility	K_{oc} = 27 Very high mobility
Loamy sand (East Anglia, United Kingdom)	K_{oc} = 360 Moderate mobility	K_{oc} = 33 Very high mobility	—	—

Soil	Azoxystrobin	Reference Compound 2[b]	Reference Compound 28[c]	Reference Compound 30[c]
Loamy sand (ERTC, United States)	K_{oc} = 1490 Low mobility	—	K_{oc} = 380 Moderate mobility	K_{oc} = 100 High mobility
Sandy clay loam (Hyde Farm, United Kingdom)	K_{oc} = 700 Low mobility	K_{oc} = 65 High mobility	K_{oc} = 170 Moderate mobility	K_{oc} = 40 Very high mobility
Silty clay loam (Nebo, United Kingdom)	K_{oc} = 760 Low mobility	K_{oc} = 560 Low mobility	—	—
Silty clay loam (NRTC, United States)	K_{oc} = 1,690 Low mobility	—	K_{oc} = 810 Low mobility	K_{oc} = 250 Moderate mobility
Silty clay loam (Wisborough Green, United Kingdom)	—	—	K_{oc} = 90 High mobility	K_{oc} = 99 High mobility
Clay loam (Pickett Piece, United Kingdom)	K_{oc} = 720 Low mobility	K_{oc} = 510 Low mobility	K_{oc} = 140 High mobility	K_{oc} = 120 High mobility

[a] Mobility classifications based on McCall et al. (1981)

[b] Major transformation product

[c] Minor transformation product

Table 3 Summary of Environmental Toxicology of Azoxystrobin and its Transformation Products

Species	Study Type	Results and Interpretation
Azoxystrobin		
Earthworms (*Eisenia foetida*)	Soil contact	14-d LC_{50} = 283 mg a.i./kg soil (nominal) 14-d NOEC = 180 mg a.i./kg soil (nominal)
Honey bees (*Apis mellifera*)	Acute contact Acute oral	48-h LD_{50} > 200 µg a.i./bee (nominal) 48-h LD_{50} > 25 µg a.i./bee (nominal) relatively nontoxic[a]
Freshwater flea (*Daphnia magna*)	Acute toxicity	48-h EC_{50} = 280 µg a.i./L (analytical) 48-h NOEC = 126 µg a.i./L (analytical) highly toxic[b]
Freshwater flea (*Daphnia magna*)	Chronic toxicity	21-d LC_{50} = 150 µg a.i./L (analytical) 21-d NOEC = 44 µg a.i./L (analytical)
Rainbow trout (*Onchorynchus mykiss*)	Acute toxicity	96-h LC_{50} = 0.47 mg a.i./L (analytical) 96-h NOEC = 0.068 mg a.i./L (analytical) highly toxic[c]

Species	Study Type	Results and Interpretation
Bluegill sunfish (*Lepomis macrochirus*)	Acute toxicity	96-h LC_{50} = 1.1 mg a.i./L (analytical) 96-h NOEC = 0.50 mg a.i./L (analytical) moderately toxic[c]
Fathead minnow (*Pimephales promelas*)	Early life cycle toxicity	28-d LOEC = 193 µg a.i./L (analytical) 28-d NOEC = 147 µg a.i./L (analytical)
Bobwhite quail (*Colinus virginianus*)	Single dose oral toxicity	LD_{50} > 2130 mg/kg bw (analytical) NOEC = 2130 mg/kg bw (analytical) practically nontoxic[d]
Bobwhite quail (*Colinus virginianus*)	5-d dietary toxicity	LC_{50} > 5290 mg/kg feed (analytical) NOEC = 5290 mg/kg feed (analytical) practically nontoxic[e]
Mallard duck (*Anas platyrhynchos*)	5-d dietary toxicity	LC_{50} > 5290 mg/kg feed (analytical) NOEC = 2550 mg/kg feed (analytical) practically nontoxic[e]
Mallard duck (*Anas platyrhynchos*)	Reproduction	NOEC = 1200 mg/kg feed (nominal) LOEC = 3000 mg/kg feed (nominal)
Mouse	90-d dietary toxicity	NOEC = 100 mg/kg feed
Rat	90-d dietary toxicity	NOEC = 200 mg/kg feed
Mouse	2-year dietary toxicity	NOEC = 300 mg/kg feed
Rat	2-y dietary toxicity	NOEC = 300 mg/kg feed
Rat	Multi-generation reproduction	NOEC = 300 mg/kg feed
Freshwater diatom (*Navicula pelliculosa*)	Biomass curve area Growth rate	E_bC_{50} = 57 µg/L (nominal) E_rC_{50} > 320 µg/L (nominal) NOEC = 20 µg/L (nominal)
Blue-green algae (*Anabaena flos-aquae*)	Biomass curve area, growth rate	NOEC = 8.5 mg/L (analytical)
Green algae (*Selenastrum capricornutum*)	Biomass curve area Growth rate	E_bC_{50} = 120 µg/L (nominal) E_rC_{50} = 1400 µg/L (nominal) NOEC = 25 µg/L (nominal)
Duckweed (*Lemna gibba*)	Frond growth Dry weight	14-d EC_{50} = 3.2 mg/L (nominal) NOEC = 0.8 mg/L (nominal) 14-d EC_{50} > 6.4 mg/L (nominal) NOEC = 3.2 mg/L (nominal)
Carrot (*Daucus carota*)	Seedling emergence Dry weight	EC_{25}, EC_{50} > 2240 g product/ha (1120 g a.i./ha)[f] NOEC = 2240 g product/ha (1120 g a.i./ha)[f] EC_{25}, EC_{50} > 1120 g product/ha (560 g a.i./ha)[f] NOEC = 1120 g product/ha (560 g a.i./ha)[f]

Species	Study Type	Results and Interpretation
Reference Compound 2		
Freshwater flea (*Daphnia magna*)	Acute toxicity	48-h EC_{50} > 180 mg/L (nominal) 48-h NOEC = 32 mg/L (nominal) practically nontoxic[b]
Rainbow trout (*Onchorynchus mykiss*)	Acute toxicity	96-h LC_{50} > 150 mg/L (analytical) 96-h NOEC = 150 mg/L (analytical) practically nontoxic[d]
Green algae (*Selenastrum capricornutum*)	Biomass curve area Growth rate	E_bC_{50} = 47 mg/L (analytical) E_rC_{50} = 80 mg/L (analytical) NOEC = 32 mg/L (analytical)

a Toxicity classification based on Atkins et al. (1981)

b Toxicity classification based on USEPA (1985c)

c Toxicity classification based on USEPA (1985d)

d Toxicity classification based on USEPA (1985a)

e Toxicity classification based on USEPA (1985b)

f Product = HERITAGE Fungicide 50WG formulation; all values reported as nominal concentrations

Table 4 Risk Characterization: Terrestrial Plants and Earthworms

Species	Toxicity Endpoint	EEC	Risk Quotient (EEC/toxicity endpoint)	Risk Classification
Azoxystrobin: Toxicity Endpoints				
Earthworms	NOEC = 180 mg a.i./kg soil	0.000 14 mg a.i./kg soil	0.000 000 78	Negligible
Terrestrial plants (seedling emergence)	NOEC = 560 g a.i./ha	0.32 g a.i./ha	0.000 57	Negligible

Table 5 Toxicity Endpoints: Study Endpoint, Dose-based Endpoint, and Dose-based Endpoint Used in Risk Characterization for Birds and Wild Mammals

Test Species	Study Type	Results and Interpretation	Toxicity Endpoint - Dose-based	Toxicity Endpoint Used in Risk Assessment
Bobwhite quail	Single dose oral	LD_{50} > 2130 mg/kg bw (analytical) NOEL = 2130 mg/kg bw (analytical) practically nontoxic	LD_{50} > 2130 mg/kg bw NOEL = 2130 mg/kg bw	NOEL = 2130 mg/kg bw (LD_{50} > 2130 mg/kg bw)

Test Species	Study Type	Results and Interpretation	Toxicity Endpoint - Dose-based	Toxicity Endpoint Used in Risk Assessment
Bobwhite quail	5-d dietary	LC_{50} > 5290 mg/kg feed (analytical) NOEC = 5290 mg/kg feed (analytical) practically nontoxic	LD_{50} > 562 mg a.i./kg bw/day[a] NOEL = 562 mg a.i./kg bw/day[a]	NOEL = 144 mg a.i./kg bw/day
Mallard duck	5-d dietary	LC_{50} > 5290 mg/kg feed (analytical) NOEC = 2550 mg/kg feed (analytical) practically nontoxic	LD_{50}> 299 mg a.i./kg bw/day[a] NOEL = 144 mg a.i./kg bw/day[a]	
Mallard duck	Reproduction	NOEC = 1200 mg/kg feed (nominal)	NOEL = 196 mg a.i./kg bw/day[b]	NOEL = 196 mg a.i./kg bw/day
Mouse	90-d dietary	NOEC = 100 mg/kg feed	NOEL = 17 mg/kg bw/day[c]	NOEL = 17 mg/kg bw/day
Rat	90-d dietary	NOEC = 200 mg/kg feed	NOEL = 20 mg/kg bw/day[c]	
Rat	Multi-generation reproduction	NOEC = 300 mg/kg feed	NOEL = 34 mg/kg bw/day[c]	NOEL = 34 mg/kg bw/day

a For conversion to dose based toxicity endpoint, the following parameters were used for food consumption and body weight:

Food Consumption (FC) (Nagy, 1987): All birds equation: FC (g dw/day) = 0.648 (BW in g)$^{0.651}$

Average body weight (Dunning, 1993): adult mallard: 1082 g; adult bobwhite: 178 g

Conversion: NOEL (mg a.i./kg bw/day) = NOEC (mg a.i./kg feed) x FC (kg dw/day) ÷ BW (kg bw)

b As reported in toxicity study (DACO 9.6.3.2, PMRA Document 1178024): 1200 mg/kg diet estimated as 196 mg/kg bw/day

c Regulatory Note REG2000-15

Table 6 Toxicity Endpoints Expressed in Terms of the Number of Seeds Consumed to Reach the Toxicity Endpoint for Each Size Class of Birds and Mammals

Species and Body Weight	Toxicity Test Exposure	Toxicity Endpoint	Toxicity Endpoint in # Seeds (per day) to Reach to Toxicity Endpoint [Toxicity endpoint (mg a.i./kg bw/day) × BW (kg bw) ÷ 0.0038 mg a.i./seed]
Small bird (20 g)	Acute oral-single dose	NOEL = 2130 mg a.i./kg bw (LD_{50} > 2130 mg a.i./kg bw) Adjusted LD_{50}, NOEL[a]: 1530 mg a.i./kg bw	NOEL = 8053 seeds (LD_{50} > 8053 seeds)
	5-day dietary	NOEL = 144 mg a.i./kg bw/day	NOEL = 758 seeds/day
	Reproduction	NOEL = 196 mg a.i./kg bw/day	NOEL 1032 seeds/day
Medium bird (100 g)	Acute oral	NOEL = 2130 mg a.i./kg bw (LD_{50} > 2130 mg a.i./kg bw) Adjusted LD_{50}, NOEL[a]: 1953 mg a.i./kg bw	NOEL = 51395 seeds (LD_{50} > 51395 seeds)
	5-day dietary	NOEL = 144 mg a.i./kg bw/day	NOEL = 3789 seeds/day
	Reproduction	NOEL = 196 mg a.i./kg bw/day	NOEL = 5158 seeds/day
Large bird (1000 g)	Acute oral	NOEL = 2130 mg a.i./kg bw (LD_{50} > 2130 mg a.i./kg bw) Adjusted LD_{50}, NOEL[a]: 2759 mg a.i./kg bw	NOEL = 726 052 seeds (LD_{50} > 726 052 seeds)
	5-day dietary	NOEL = 144 mg a.i./kg bw/day	NOEL = 37 895 seeds/day
	Reproduction	NOEL = 196 mg a.i./kg bw/day	NOEL = 51 579 seeds/day
Small mammal (15 g)	90-day dietary	NOEL = 17 mg a.i./kg bw/day	NOEL = 67 seeds/day
	Multi-generation reproduction	NOEL = 34 mg a.i./kg bw/day	NOEL = 134 seeds/day
Medium mammal (35 g)	90-day dietary	NOEL = 17 mg a.i./kg bw/day	NOEL = 156 seeds/day
	Multi-generation reproduction	NOEL = 34 mg a.i./kg bw/day	NOEL = 313 seeds/day

Species and Body Weight	Toxicity Test Exposure	Toxicity Endpoint	Toxicity Endpoint in # Seeds (per day) to Reach to Toxicity Endpoint [Toxicity endpoint (mg a.i./kg bw/day) × BW (kg bw) ÷ 0.0038 mg a.i./seed]
Large mammal (1000 g)	90-day dietary	NOEL = 17 mg a.i./kg bw/day	NOEL = 4474 seeds/day
	Multi-generation reproduction	NOEL = 34 mg a.i./kg bw/day	NOEL = 8947 seeds/day

[a] The acute single-dose oral toxicity endpoint was adjusted for the relationship between toxicity and body weight (Mineau, et al., 1996): $LD_{50}(2) = (W2/W1)^{b-1} \times LD_{50}(1)$ where b = 1.15 (for birds); b = 0.75 for mammals

Table 7 Estimated Dietary Exposure: Birds and Wild Mammals

Species and Size	Food Ingestion (FI) g dw/day[a]	Corn Seeds Consumed per Day (100% food as seeds) [FI x 2.632 seeds/g]	Maximum Number of Seeds per Area of Planted Field
Small bird (20 g)	5.08 g dw/day	13.4 seeds/day	8.4 seeds/m^2
Medium bird (100 g)	19.9 g dw/day	52.5 seeds/day	8.4 seeds/m^2
Large bird (1000 g)	58.1 g dw/day	153 seeds/day	8.4 seeds/m^2
Small mammal 15 g	2.18 g dw/day	5.74 seeds/day	8.4 seeds/m^2
Medium mammal 35 g	4.37 g dw/day	11.5 seeds/day	8.4 seeds/m^2
Large mammal 1000 g	68.7 g dw/day	181 seeds/day	8.4 seeds/m^2

[a] Food ingestion is calculated using the allometric equations below (Nagy, 1987).

For generic bird weights less than or equal to 200 g, the equation for "passerine" birds was used, for bird weights more than 200 g, the equation for "all birds" was used. For mammals, the equation for "all mammals" was used. Food ingestion is calculated in terms of g dry weight of food per day. As a conservative estimate, treated seed is assumed to be equivalent to dry weight of food as minimal moisture is expected to be present in treated seeds ready for planting.

Passerines: $FI\ (g\ dw/day) = 0.398\ (BW\ in\ g)^{0.850}$

All birds: $FI\ (g\ dw/day) = 0.648\ (BW\ in\ g)^{0.651}$

All mammals: $FI\ (g\ dw/day) = 0.235\ (BW\ in\ g)^{0.822}$

Table 8 Risk Characterization: Birds and Wild Mammals

Species and Body Weight	Toxicity Test Exposure	Toxicity Endpoint in # Seeds (per day)	Estimated Daily Exposure in # Seeds (per day)	RQ (exposure/ toxicity)	Risk Classification
Small bird (20 g)	Acute oral-single dose	NOEL = 8053 seeds (LD_{50} > 8053 seeds)	13.4 seeds/day	0.002	Negligible
	5-day dietary	NOEL = 758 seeds/day	13.4 seeds/day	0.018	Negligible
	Reproduction	NOEL = 1032 seeds/day	13.4 seeds/day	0.013	Negligible
Medium bird (100 g)	Acute oral	NOEL = 51 395 seeds (LD_{50} > 51 395 seeds)	52.5 seeds/day	0.001	Negligible
	5-day dietary	NOEL = 3789 seeds/day	52.5 seeds/day	0.014	Negligible
	Reproduction	NOEL = 5158 seeds/day	52.5 seeds/day	0.010	Negligible
Large bird (1000 g)	Acute oral	NOEL = 726 052 seeds (LD_{50} > 726 052 seeds)	153 seeds/day	< 0.001	Negligible
	5-day dietary	NOEL = 37 895 seeds/day	153 seeds/day	0.004	Negligible
	Reproduction	NOEL = 51 579 seeds/day	153 seeds/day	0.003	Negligible
Small mammal (15 g)	90-day dietary	NOEL = 67 seeds/day	5.74 seeds/day	0.086	Negligible
	Multi-generation reproduction	NOEL = 134 seeds/day	5.74 seeds/day	0.043	Negligible
Medium mammal (35 g)	90-day dietary	NOEL = 156 seeds/day	11.5 seeds/day	0.074	Negligible
	Multi-generation reproduction	NOEL = 313 seeds/day	11.5 seeds/day	0.037	Negligible
Large mammal (1000 g)	90-day dietary	NOEL = 4,474 seeds/day	181 seeds/day	0.040	Negligible
	Multi-generation reproduction	NOEL = 8,947 seeds/day	181 seeds/day	0.020	Negligible

Table 9 Risk Characterization: Aquatic Organisms

Species	Toxicity Endpoint	EEC	Risk Quotient (EEC/NOEC)	Risk Classification
Azoxystrobin: Acute Toxicity Endpoints				
Daphnia magna	NOEC = 0.126 mg a.i./L	0.000 107 mg a.i./L	0.000 9	Negligible
Rainbow trout	NOEC = 0.068 mg a.i./L	0.000 107 mg a.i./L	0.001 6	Negligible
Bluegill sunfish	NOEC = 0.5 mg a.i./L	0.000 107 mg a.i./L	0.000 2	Negligible
Navicula pelliculosa	NOEC = 0.020 mg a.i./L	0.000 107 mg a.i./L	0.005 4	Negligible
Anabaena flos-aquae	NOEC = 8.5 mg a.i./L	0.000 107 mg a.i./L	0.000 01	Negligible
Selenastrum capricornutum	NOEC = 0.025 mg a.i./L	0.000 107 mg a.i./L	0.004 3	Negligible
Lemna gibba	NOEC = 0.8 mg a.i./L	0.000 107 mg a.i./L	0.000 1	Negligible
Azoxystrobin: Chronic Toxicity Endpoints				
Daphnia magna	NOEC = 0.044 mg a.i./L	0.000 107 mg a.i./L	0.002 4	Negligible
Fathead minnow	NOEC = 0.147 mg a.i./L	0.000 107 mg a.i./L	0.000 7	Negligible
Reference Compound 2: Acute toxicity end points				
Daphnia magna	NOEC = 32 mg a.i./L	0.000103 mg/L[a]	0.000 003 2	Negligible
Rainbow trout	NOEC = 150 mg a.i./L	0.000103 mg/L[a]	0.000 000 7	Negligible
Selenastrum capricornutum	NOEC = 32 mg a.i./L	0.000103 mg/L[a]	0.000 003 2	Negligible

[a] EEC for Reference Compound 2 is 0.000103 mg/L assuming 100% conversion of azoxystrobin to Reference Compound 2 and correcting for molecular weight. Calculation: [0.000107 mg a.i./L x (389.4 g/mol Reference Compound 2) / (403.4 g/mol azoxystrobin) = 0.000103 mg/L]

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